UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,890	08/28/2000	Oliver Brustle	V0S-012	7106

23483 7590 08/14/2006

WILMER CUTLER PICKERING HALE AND DORR LLP
60 STATE STREET
BOSTON, MA 02109

EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,890	BRUSTLE, OLIVER	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *106-136* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *106-136* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 June 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/1/06 & 5/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed May 1, 2006 has been entered. Claims 2, 3, 6, 8-12, 15, 46-48, 50, 76-83, 85-94, and 96-104 have been cancelled. Claims 106-136 have been newly added.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 1, 2006 has been entered.

The rejection of the prior pending claims under 35 U.S.C. 112, first paragraph, for lack of enablement is withdrawn in view of the cancellation of these claims. The rejection has not been applied to the newly added claims in view of the new claim language, and further in view of the Declaration of Dr. Bruestle, which argues that cell compositions consisting essentially of different proportions of embryonic stem cell-derived neural precursor cells, and neuronal or glial cells derived from the embryonic stem cell-derived neural precursor cells, could be obtained by one of skill in the art based on the disclosure in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Pharmaceutical Compositions

Claims 115, 125, and 134 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record set forth in the Office Actions of 4/21/04 and 12/2/05, as applied to Claim 97, because the specification, while being enabling for pharmaceutical compositions comprising neuronal cells, does not reasonably provide enablement for pharmaceutical compositions comprising glial cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 115, 125, and 134 are directed to a pharmaceutical composition. The claims cover glial cell compositions.

Insofar as the claims continue to cover glial cell compositions as pharmaceutical compositions, the claims are rejected for lack of enablement. As noted below, and in the prior Office Action mailed 12/2/05, pharmaceutical compositions comprising neuronal cells are considered to be enabled.

At pages 17-18 of the response, with regard to the rejection of Claims 46, 86, 97, and 99 for lack of an enabling disclosure for producing a therapeutic effect upon transplantation of the claimed cell compositions (i.e., the intended use of the claimed pharmaceutical compositions), Applicant asserts that Example 4 provides a therapeutic use for transplanting oligodendroglial/astrocytic precursors into myelin-deficient rats for the purpose of myelin regeneration. However, there is nothing in Example 4 that points to a therapeutic outcome and Applicant provides no support for the assertion that Example 4 provides a therapeutic use. Although donor mouse cells were detected in the rat brain following embryonic transplantation, no therapeutic effect was demonstrated. Applicants assert that the remyelination would be considered therapeutic. No support is offered for this assertion.

The rejection of Claims 46, 86, and 99 under 35 U.S.C. 112, first paragraph, for failing to provide an enabling disclosure for a pharmaceutical use of the claimed invention, was withdrawn in view of Applicant's arguments relating to Example 5.2, as set forth at pages 14-16 of the response of October 22, 2004. The Examiner acknowledges that transplantation of mouse ES cell-derived neural cell compositions into adult rat brain with ibotenic acid-induced striatal lesions resulted in reduced amphetamine-induced rotational behavior. However, these cell compositions were neuronal cell compositions, not glial cell compositions.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 115, 125, and 134 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 115 is indefinite in its recitation of "the precursor cells of claim 106" because Claim 106 is directed to an isolated, non-tumorigenic cell composition, not precursor cells.

Claim 125 is indefinite in their recitation of "the precursor cells of claim 118" because Claim 118 is directed to an isolated, non-tumorigenic cell composition, not precursor cells.

Claim 134 is indefinite in its recitation of "the precursor cells of claim 126" because Claim 126 is directed to a cell composition, not precursor cells.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application

> by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 106-136 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 5,980,885 (Weiss et al., 1999; filed June 7, 1995), for reasons of record as applied to the previously pending claims.

The claims have been amended so that they are now directed to cell compositions claimed in a product-by-process format. The claims cover heterogeneous cell compositions comprising neural precursor cells and other types of differentiated neural cells.

The instant claims are product-by-process claims. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. The patentability of a product does not depend on its method of production. See M.P.E.P. 2113. Thus, the claims read on neural stem cells disclosed in the prior art, for the reasons set forth herein below.

Weiss et al. (1999) disclose mammalian neural stem cells. These cells can be derived from embryonic, juvenile, or adult mammalian neural tissue. The cells can be induced to differentiate into neurons, astrocytes, and oligodendrocytes. Although the instantly claimed cells are limited to cells derived from embryonic stem cells, no particular identifying characteristics are recited in the claims other than the requirement that the cells differentiate into "neuronal cells or glial cells" or just "glial cells." The cells disclosed by Weiss et al. satisfy this limitation. Weiss

et al. further disclose that the neural stem cells form neurospheres in suspension culture (Columns 33-34). The specification particularly states that "[i]n the continued presence of a proliferation-inducing growth factor such as EGF or the like, precursor cells within the neurosphere continue to divide resulting in an increase in the size of the neurosphere and the number of undifferentiatated cells." Example 6, *inter alia*, provides a disclosed embodiment of a cell composition comprising 100% neural cells and neural precursor cells, as instantly claimed. The example discloses that neurospheres were dissociated and single cells from the dissociated neurospheres were suspended in tissue culture flasks. A percentage of dissociated cells began to proliferate and formed new neurospheres largely composed of undifferentiated cells. Thus, both the starting material (i.e., the single cell suspension) and the final culture of Example 6 represent cell compositions as claimed. The reference further discloses that the neural stem cells are non-tumorigenic (Column 1, lines 39-44) and can be used for autologous transplantation (Column 1, lines 49-50).

In the absence of evidence to the contrary, the neural stem cell compositions disclosed by Weiss et al. are indistinct from the cell compositions instantly claimed.

Thus, the claimed compositions are disclosed in the prior art.

The Declaration of Dr. Brustle has been fully considered but is not found to be persuasive as it pertains to the rejection under 35 U.S.C. 102(e). The Declaration asserts that the embryonic stem cells, as well as the neural precursor cells derived therefrom, are not as lineage-restricted as the neural stem cells of Weiss et al. The Declarant concludes that the claimed compositions are therefore different from Weiss et al. However, the claimed compositions are very broad in scope, covering compositions comprising any type of neural precursor cell in combination with any type of neuron or any type of glial cell. The presence of the purported less lineage-restricted neural precursor cell is not a limitation of the claims. Thus, Applicants are arguing limitations that are not in the claims. The Declaration seems to suggest that the methods recited in the instant claims could not possibly produce a single embodiment of the cell compositions as disclosed by Weiss et

al. However, given that the claims cover the use of any type of growth factor in three sequential culturing steps, for any length of time, and further given that the precursor cells used to produce the instant compositions allegedly have **greater** potentiality than neural stem cells isolated from neural tissue, as the Declarant contends, it is maintained that the instant claims encompass the cell compositions disclosed by Weiss et al.

Conclusion

No claims are allowable.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are

available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER